

REMARKS

The Examiner is kindly thanked for the courtesies extended to Applicants' representative during a telephonic interview on August 3, 2004, during which the propriety of the various restrictions, and the designation of the various claims was discussed.

Applicants also ask the Examiner to note the current attorney docket number for the instant application, *i.e.*, 61040-0013, and to ensure that the Office records are updated in this respect for future correspondence.

Amendments to the Claims

Claims 1–25, 29–35, and 39–141 are pending in the instant application. With the instant amendment, Applicants amend claims 45, 47, and 51 to correct various informalities of dependency and antecedent basis. Applicants further amend claim 136 to delete the term ligand, and replace it with agonist. Support for this amendment can be found in Example 1 of the specification as filed, at pages 35–41.

Applicants also introduce new claims 142 – 144, and 148 which find support in the specification as filed, in Examples 3 and 4, at pages 42 – 44.

Applicants also introduce new claims 145 – 147, depending from claim 44, each reciting a resolution value of the cocrystal structure that is found in the specification as filed, page 26, at lines 7 – 9.

No new matter is introduced by the instant amendments and, accordingly, entry thereof is respectfully requested.

The Restriction Requirement

Applicants have considered the office action mailed June 25, 2004 in connection with the above-identified patent application. The Examiner has required restriction of the pending claims under 35 U.S.C. § 121 to one of the following ten groups:

Group I. Claims 1-24, 72-133, and 140-141, drawn to methods of identifying compounds which modulate nuclear receptor activity or modulate binding of a ligand to a nuclear receptor.

Group II. Claims 29-33, drawn to a method of modulating nuclear receptor activity in a mammal.

Group III. Claims 34-35 and 39, drawn to a machine readable storage medium capable of graphical three-dimensional representation.

Group IV. Claims 40-43, drawn to a machine readable storage medium comprising a program for correspondence of data.

Group V. Claims 44-48, drawn to a crystal comprising a portion of an estrogen receptor and an agonist.

Group VI. Claims 49-51, drawn to a crystal comprising a portion of an estrogen receptor and an antagonist.

Group VII. Claims 52-66, drawn to a computational method of designing a nuclear receptor ligand.

Group VIII. Claims 67-71, drawn to a method of modulating nuclear receptor activity in a mammal by administering a chemically modified ligand.

Group IX. Claims 134-135, drawn to a method of modulating nuclear receptor activity in a mammal by administering an antagonist.

Group X. Claims 136-139, drawn to an isolated protein complex.

Applicants hereby point out that claim 25 has been omitted from the list of restricted claims in the office action mailed June 25, 2004. Applicants also point out that claim 50 has been incorrectly placed in Group VI. Because claim 50 depends from claim 44, it should properly be placed in Group V. The Examiner is also thanked for acknowledging during the telephonic interview on August 3, 2004 that these matters are merely typographical errors and for giving Applicants the opportunity to correct the record.

Applicants also respectfully request a provisional assignment of new claims 142 – 148 based on their respective dependencies, to groups V and X, as follows:

Claims 142 – 147: **Group V.**

Claim 148: **Group X**

Accordingly, Applicants submit that Groups I, V, VI and X should be designated as follows, pending reconsideration of the restriction requirement in light of the partial traversal hereinbelow:

Group I. Claims 1–25, 72-133, and 140–141, drawn to methods of identifying compounds which modulate nuclear receptor activity or modulate binding of a ligand to a nuclear receptor.

Group V. Claims 44–48, 50, and 142 – 147, drawn to a crystal comprising a portion of an estrogen receptor and an agonist.

Group VI. Claims 49 and 51, drawn to a crystal comprising a portion of an estrogen receptor and an antagonist.

Group X. Claims 136–139, and 148, drawn to an isolated protein complex.

The Examiner is also thanked for a suggested form of amendment that would facilitate joinder of Groups V and X for the purpose of examination on the merits, as further discussed hereinbelow.

Provisional Election

The present response is intended to be fully responsive to the restriction requirement issued by the Examiner. Applicants respectfully request joinder of Groups X and V in light of the amendments herein, and, accordingly, provisionally elect to prosecute concurrently the claims of **Groups V and X**. In the event that the Examiner is unable to join such groups, Applicants hereby provisionally elect to prosecute the claims of **Group V**, drawn to a cocrystal comprising a portion of an estrogen receptor having an agonist and a coactivator bound thereto.

Notwithstanding the foregoing provisional election, Applicants respectfully traverse the Examiner's restrictions with respect to certain groups.

Partial Traversal

With respect to the Examiner's division of the instant claims into 10 groups and the reasons stated therefor, Applicants respectfully traverse. In doing so, Applicants remind the Examiner that the instant application is a national phase application of International application serial no. PCT/US99/06937. Thus, Applicants respectfully point out that the Examiner must adopt the "Unity of Invention" standard applicable to international applications, as the guiding principle for considering whether it is reasonable to restrict various groups of claims. *Caterpillar Tractor Co. v. Commissioner of Patents and Trademarks*, 231 USPQ 590 (holding that PTO interpretation of 37 CFR § 1.141(b)(2) as applied to unity of invention determinations in international applications is not in accordance with PCT regulations). Even though a search report did not issue in connection with the aforementioned international application, the Examiner must still apply the Unity of Invention standard under PCT Rule 13.2 in respect of the instant claims. *See* MPEP § 1850.

Under PCT Rule 13.2, Unity of invention exists where there is a technical relationship among the claimed inventions that involves one or more "special technical features." A special technical feature is a common concept that each of the inventions, considered as a whole, makes over the prior art.

Applicant respectfully submits that claims in **Groups I, II, III, VII and VIII** possess the following special technical features:

an atomic structural model of the estrogen receptor ligand binding domain, comprising atomic coordinates of:
 helix 12 of the ligand binding domain;
 a coactivator binding site, and
 a coactivator bound to the coactivator binding site.

Accordingly, Applicants respectfully request joinder of **Groups I, II, III, VII and VIII**, when conducting future prosecution of the subject Application.

Applicants point out that the foregoing arguments are not be construed as an admission that the claims of any of groups I, II, III, VII and VIII are obvious over, or are not partentably distinct from, the claims of any other of such groups.

Furthermore, Applicants respectfully submit that claims in **Groups V and X** (as amended herein) possess the following special technical feature:

a protein structure comprising:
 an estrogen receptor ligand binding domain;
 a ligand bound to the ligand binding domain; and
 a coactivator bound to the coactivator binding site.

Accordingly, Applicants respectfully request joinder of **Groups V and X** when conducting future prosecution of the subject Application.

Applicants point out that the foregoing arguments are not be construed as an admission that the claims of either of group V are obvious over, or are not partentably distinct from, the claims of group or X, or vice versa.

Applicants also take this opportunity to point out that, by arguing for a unity of invention standard to be applied to the instant claims, Applicants do not accept the force or validity of any of the Examiner's arguments in respect of the form of restriction requirement issued in her Office Action mailed June 25, 2004.

In summary, for the reasons discussed hereinabove, Applicants respectfully request that the restriction of these claims be reconsidered and applied in accordance with the framework set forth herein. Applicants retain the right to petition from the restriction requirement under 37 C.F.R. § 1.144.

CONCLUSION

Applicants respectfully request that the above-made remarks be made of record in the file history of the present application. Applicants have presented a request that **Groups V and X** be joined and have made a provisional election of the same, with a partial traverse

with respect to Groups I, II, III, VII, and VIII, as well as to groups V and X. In the event that such a traverse is not deemed persuasive, Applicants provisionally elect **Group V** for prosecution.

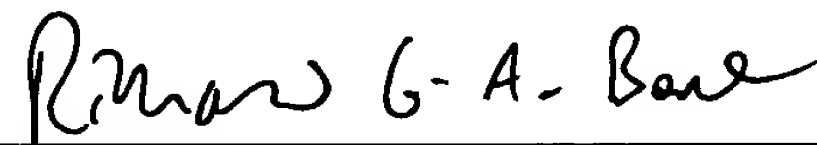
If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 843-4000.

No fee is believed owed in connection with filing of this amendment and response, other than the petition for extension of time fee, and claim fee, as authorized on separate sheets accompanied herewith. However, should the Commissioner determine otherwise, the Commissioner is authorized to charge any underpayment or credit any overpayment to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 for the appropriate amount. A copy of this sheet is attached.

Respectfully submitted,

Date: August 19, 2004

By:



Richard G. A. Bone

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(Copy of Certificate attached hereto)

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